Medical Science

25(114), August, 2021

Post covid fatal antibody dependent enhancement of dengue infection in a young male: Double trouble

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To Cite:
Beig I, Talwar D, Kumar S, Acharya S, Hulkoti V. Post covid fatal antibody dependent enhancement of dengue infection in a young male: Double trouble. Medical Science, 2021, 25(114), 1910-1914

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Peer-Review History
Received: 29 June 2021
Reviewed & Revised: 30/June/2021 to 25/July/2021
Accepted: 26 July 2021
Published: August 2021

Peer-review Method
External peer-review was done through double-blind method.

ABSTRACT

Antibodies against Dengue virus (DENV) have been postulated to act against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV 2) which might reduce the severity of COVID19 in a patient who previously had dengue fever. However, we report a case of 30 year old male who presented with dengue shock syndrome two months after contracting COVID19. The patient had no history of dengue fever in the past and had no IgG antibodies against Dengue Virus whereas he tested positive for IgG SARS CoV 2 antibodies. Therefore, we highlight a rare case of Antibody Dependent Enhancement of Dengue fever as a result of antibodies against SARS CoV2 in a young male which proved to be fatal. In our knowledge this is the first case in the world to report dengue shock syndrome as a result of SARS CoV2 antibodies.

Keywords: Dengue fever, COVID19, SARS CoV2

1. INTRODUCTION

Dengue Virus (DENV) is members of the flaviviridae family and has four different serotypes DENV1, DENV2, DENV3 and DENV4. They can cause the classical dengue fever, dengue hemorrhagic fever as well as dengue shock syndrome (Papalkar et al., 2019). Dengue fever is leading cause of mortality in the developing countries. Dengue fever typically presents as fever, rash, retro orbital pain, pain in the abdomen and nausea. Inoculation of the virus by the aedesagypti mosquito leads to infection of the local antigen presenting cells which are macrophage and dendritic cells followed by infection of the bloodstream. Laboratory parameters typically reveal leukopenia along with thrombocytopenia. After some day's antibodies are formed against the virus eliminating the viral infection. This humoral response of the immune system forms serotype specific antibodies which do cross react with other serotypes but does not provide protection against infection from other serotypes.

Reinfection with different serotype of dengue virus predisposes the patient to have enhanced reaction from the virus through FcgR-mediated virus uptake. Previous infection with dengue virus has been postulated to be

protective against COVID19 and there have also been reports of cross reactivity of COVID19 and dengue antibodies leading to false positive dengue tests in COVID19 patients. However, role of COVID19 antibodies in augmenting dengue related complications owing to the cross reactivity amongst dengue and COVID19 antibodies is not yet studied. COVID19 has emerged as an alarming scare for countries throughout the world with increased burden on healthcare facilities (Jain et al., 2020).

As dengue is a major health hazard in the developing countries, the ongoing pandemic has added an additional burden to the health care forces due to the similarity in presentation of COVID19 infection and dengue and the challenges faced to diagnose co infection owing to the false positive results witnessed. We present a rare case of 30 year old young male who contracted dengue fever two months after getting COVID19 leading to fatal dengue shock syndrome.

2. CASE PRESENTATION

A 30 year old presented to the emergency department with the chief complaint of fever along with chills for four days and red colour spots over the lower limb since two days. He also had history of headache, pain abdomen, nausea and two episodes of vomiting since one day. There was no history cough, sorethroat, burning micturition, seizure or loss of consciousness. There was no history of Dengue Fever in the past. Patient had history of COVID19 infection two months back. There was no history of Diabetes Mellitus, Hypertension, tuberculosis or bronchial asthma. On examination patient's pulse was 104 beats per minute, regular, blood pressure was 80/50mmhg in right arm supine position, tourniquet test was positive, there were petechial spots present on bilateral lower limb with pedal edema (figure 1), Fundus examination revelaed no evidence of papilledema and spo2 was 92 percent on room air.

On systemic examination chest was bilaterally clear, abdomen was soft with tenderness present in right hypochondrium and liver was palpable. Heart sounds were normal with no murmurs and patient was conscious and oriented. Patient was admitted in the intensive care unit and blood investigations revealed deranged liver and renal function test along with thrombocytopenia (table 1). He tested positive for NS1 antigen and antibody titer for Dengue IgG was negative however IgM antibody for dengue virus was positive. He also tested positive for IgM antibodies against SARS CoV 2. Patient was transfused with five units of platelets and was started on inotropic support, antibiotics, intravenous fluids and oxygen therapy. During the course of hospital stay patient's condition deteriorated further and he was intubated and taken on mechanical ventilator on day two of admission. He ultimately succumbed on day three of admission.

Table 1 Showing Lab investigations of the case

Lab Investigations	Measured Value
Complete Blood Count	Haemoglobin 7.6gm/dl MCV- 31.3 fl White Blood Cells -2500/dl Platelet Count -35800/dl
Liver Function Test	Alkaline phosphatase -203 u/l Aspartate aminotransferase 15750 u/l Alanaine Aminotransferase 12376 u/l Total Protein -6.9gm/dl Albumin -3.9 gm/dl Globulin – 3/0 gm/dl Total Bilirbin -9.5mg/dl Direct bilirubin -6.4 mg/dl Indirect bilirubin -3.1 mg/dl
Renal Function Test	Urea – 65 Creatinine 5.5 Sodium -148 Potassium 5.1
D-Dimer	0.3
Sr.ferritin	1360 ng/ml
SARS CoV 2 Antibody	IgG positive,IgM negative
Dengue Antibody	IgG negative ,IgM positive
NS1 Antigen	Positive

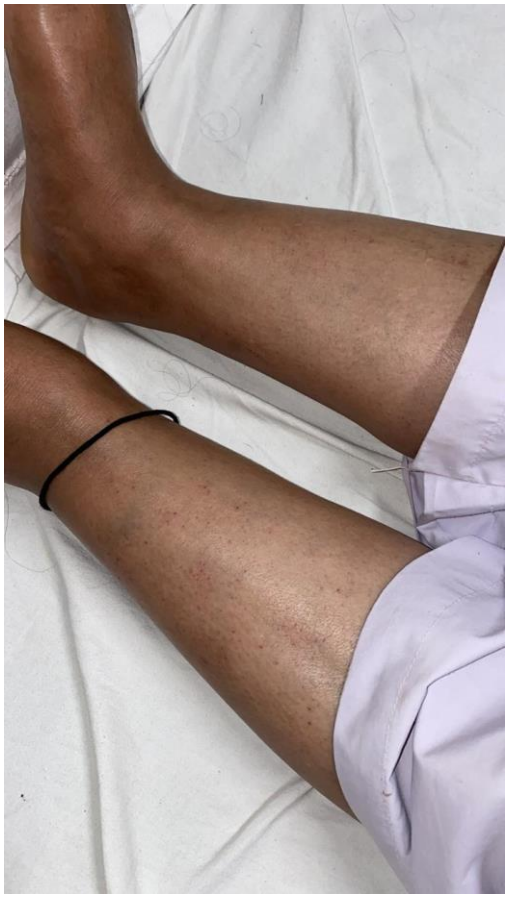

Figure 1 Showing Petechial Spots on the lower limb with pedal edema

3. DISCUSSION

The Dengue Virus has four DENV serotypes and it is an RNA virus belonging to the family of Flaviviridae. The viral particle is surrounded by lipid bilayer consisting of envelope and membrane protein (Chung et al., 2015). Dengue virus infects by attaching to a target cell and then. The virus gets engulfed inside a vacuole through the process of endocytosis. The virus then rearranges its coated proteins to bind to the memberane of the vacuole therby releasing it'sgenome and capsied into the cytoplasm where newly packaged virions are formed. This process leads to stimulation of the B cells and T cells forming antibodies. These antibodies are sepecfic for the virus.

Macrophages and monocytes then clear the antibody coated virus from the bloodstream and destroy them. However in a case of reinfection with different serotype of dengue virus the memory B cells created during the first infection form antibodies in the bloodstream which are specific to the first serotype. These antibodies are unable to bind to the new serotype of dengue virus and therefore the partially coated virions are taken up by macrophages and monocytes but are able to escape the endocytic vacuole thereby leading to infection and replication of the virus within the immune cells (zhang et al., 2020). There has been a significant overlap between COVID19 infection and Dengue fever with similar clinical presentation of fever with thrombocytopenia and cross reactivity in diagnostic testing. The serum from COVID19 patients has been shown to give false positive results for Dengue Fever by reacting with DENV Antigen (Guan et al., 2020). This cross reactivity is a double edged sword as on one hand it may prevent dengue infections in the regions with high incidence of COVID19 however it may also augment Dengue Fever through antibody dependent enhancement on the other hand leading to serious complications like dengue shock syndrome and dengue haemorrhagic fever.

A study has found that the antibodies formed against dengue envelope protein can bind to the Spike RBD amino acid residues of SARS CoV 2 therefore justifying the fact that the antibodies formed against dengue virus have some effect against SARS CoV2 which might be protective against COVID19 in patients who had contracted dengue fever in the past. It is important to note that

similar reaction may occur in individuals who have contracted COVID19 and later get infected with Dengue Fever in which case there might be improper binding of antibodies against SARS CoV2 to the Dengue virus ultimately resulting in severe complications of Dengue due to antibody dependent enhancement of dengue fever. Therefore Antibody Dependent Enhancement is an emerging challenge for individuals experiencing dengue fever for the first time in their life with history of COVID19 due to antigenic similarity between SARS CoV2 and Dengue Virus (figure 2).

In our case the patient had history of COVID19 in the recent past and had high antibody titre against SARS CoV2 however he had no prior history of Dengue Fever and He tested negative for IgG antibodies against dengue virus. In the above scenario it is likely to believe that the antibodies which were formed against SARS CoV2 may have interacted with DENV antigen leading to dengue shock syndrome in our patient.

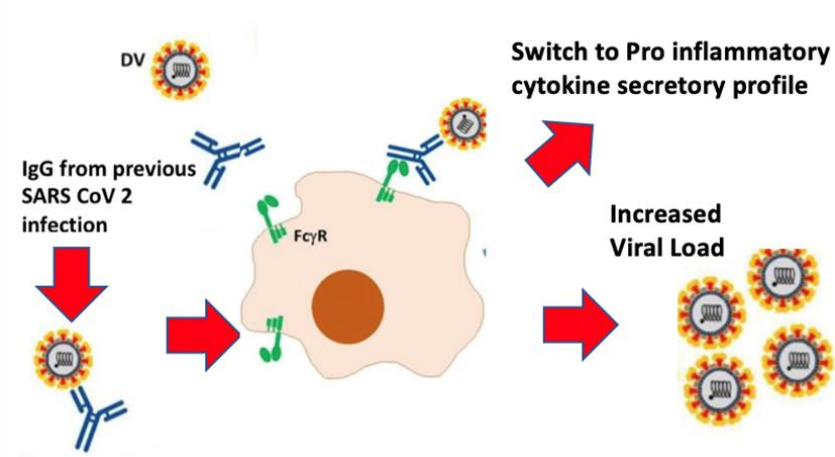

Figure 2 Pathogenesis of Dengue Shock Syndrome in Post COVID Patient

4. CONCLUSION

We conclude that in an individual with history of COVID19, dengue fever might present with unpredicted complications even in patients contracting dengue fever for the first time in their life. Therefore, clinicians treating dengue fever should be on the lookout for history of COVID19 in the past and should screen the patients for SARS CoV2 antibodies in order to prevent mortality which might result from antibody dependent enhancement of dengue fever.

Author's Contribution

All authors contributed equally to the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

Funding Source

The research has not received any external funding.

Acknowledgement

We thank the patients who participated and contributed samples to the study.

Informed Consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Data and materials availability

All data associated with this study are present in the paper.

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